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Information Bulletin

Toxoplasmosis

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Toxoplasma gondii, the causative agent of toxoplasmosis, is a protozoan parasite that infects a wide range of animal species, including cats and human beings. *Toxoplasma gondii* was discovered in 1908 in the gundi, a small African rodent, in which the protozoan produces fatal disease. Cats, domestic and wild, are the *definitive host* (host wherein the adult or sexually mature stage of the parasite is produced) of *T. gondii* and are the parasite's primary reservoir of infection throughout the world. Domestic cats are by far the most important species in transmission of *T. gondii* to other animals and to human beings.

Although the incidence of toxoplasmosis among human beings probably has not changed significantly over the last several years, an increasing awareness and concern about the disease has arisen within the medical and veterinary communities. It has been estimated that 30 percent to 50 percent of the world's human population has been exposed to *T. gondii* and harbors the clinically inapparent, chronic (cyst) form of the parasite. *Toxoplasma gondii* is of importance because, if given the opportunity, it can produce devastating disease in congenitally infected infants and immunocompromised patients. For that reason veterinarians are frequently called on to clarify the role that cats play in the transmission of *T. gondii* to human beings.

The Life Cycle of *Toxoplasma gondii*

Toxoplasma gondii is a coccidian protozoan belonging to the family Sarcocystidae. In general, sarcocystid coccidia are transmitted by the fecal-oral route and by carnivorism, reproducing within the intestine in a sequence of asexual and sexual stages that in some cases require alternate host species. *Toxoplasma gondii* requires only the cat in order to complete its complex life cycle; thus cats are both the definitive and the "complete" hosts for *T. gondii*. However, other animal species and human beings can also become involved in the infection cycle as *intermediate hosts* of the parasite.

Cats acquire *T. gondii* infection by ingesting any of the three infective stages of the parasite: *cyst* (containing *bradyzoites*), *oocyst*, and *tachyzoite*. Following ingestion of cysts (acquired from infected prey species, usually rodents), enzymes in the digestive tract of the cat break down the cyst wall and release the imprisoned bradyzoite forms, initiating the *intraintestinal* infection cycle. That cycle occurs only in members of the cat family. The lancet-shaped bradyzoites penetrate the cells lining the small intestine and initiate a metamorphic sequence of asexual reproductive stages of the parasite (*schizogony*), which progresses eventually to a sexual cycle of reproduction (*gametogony*). After each female gamete is fertilized, the resulting *zygote* is encased in a double-layered wall, forming an unsporulated oocyst. Oocysts, which can number in the millions, are then passed in the feces for about one to two weeks (see fig. 1). Within five days of excretion, the oocysts *sporulate* and become infectious to other animals. Sporulated oocysts are highly resistant to environmental conditions (freezing, drying, disinfecting solutions) and can survive in shaded soil or sand for as long as eighteen months. Subsequent ingestion of sporulated oocysts initiates intraintestinal multiplication of tachyzoite forms, which localize in tissues as cyst-imprisoned bradyzoites.

During the period of asexual reproduction, some bradyzoites released from the ingested cysts penetrate more deeply into the wall of the intestine, where they multiply as tachyzoite forms (see fig. 2). Within a very short time (hours), the banana-shaped tachyzoites can spread out from the intestinal tract to infect other body sites via the lymphatic and blood vascular systems, initiating the *extraintestinal* infection cycle. Tachyzoites are actively reproductive forms that kill infected cells essentially by bursting them: the parasites multiply rapidly and fill up the intracellular space until the infected cell ruptures. Eventually the cat's immune system restrains this stage of the organism. *Toxoplasma gondii* then enters a dormant, or "resting," stage by forming cysts within certain tissues, particularly in the brain and musculature. The extraintestinal infection cycle of *T. gondii* occurs not only in cats but also in the intermediate hosts (including human beings) of the parasite.

Tissue cysts may contain hundreds or thousands of "sleeping" bradyzoites and can remain dormant essentially for the lifetime of the host (see fig. 3). Occasionally, however, some cysts probably rupture. In some cases the newly liberated bradyzoites may revert to the tachyzoite stage and produce active disease (*toxoplasmosis*), with reshedding of oocysts. That might occur, for example, following periods of stress (pregnancy and lactation, intercurrent disease) or immunosuppressive drug therapy. Much more often, however, immune responses successfully prevent both disease and recrudescence of shedding.

The majority of healthy exposed cats, having once shed oocysts, will not shed them again. Even in those few cats that do reexcrete oocysts (following a subsequent reexposure to *T. gondii,* for example), the number of oocysts shed is smaller and may even be insufficient to effectively transmit the parasite.

Transmission of *T. gondii*

Cats Ingestion of tissue cysts present in infected prey animals or in other raw meat probably is the most common route by which cats are exposed to *T. gondii*. It is also the route that is of greatest significance in the spread of the organism, for nearly all cats shed oocysts in feces after their first ingestion of tissue cysts. By contrast, fewer than 50 percent of cats shed oocysts after their first ingestion of either oocysts (from contaminated soil) or tachyzoites (from actively diseased prey or from other

raw meat). In addition, the number of oocysts shed after oocyst ingestion is much less than the number excreted after consumption of tissue cysts. Most feral (free-roaming) cats appear to acquire their initial *T. gondii* infection shortly after weaning, probably by ingestion of infected prey. Thus, infection rates tend to be higher among feral felines than among pet cats. The *prepatent period* (the time between initial infection and the shedding of oocysts in feces) varies from three days to seven weeks, depending on the stage of the parasite that has been ingested. The period is shorter (3 to 10 days) if tissue cysts are ingested, and longer (3 to 7 weeks) if oocysts or tachyzoites are consumed.

Congenital infection—transmission of *T. gondii* from mother to offspring—is common in sheep and goats but is of much less importance in cats. In cats congenital transmission probably occurs only rarely.

Human Beings and Other Species

Sporulated oocysts of *T. gondii* can infect a number of other species and initiate the extraintestinal infection cycle. Contact with oocyst-contaminated soil is probably the major means by which many of these different species—rodents, ground-feeding birds, sheep, goats, pigs, and cattle, as well as human residents of developing countries—are exposed to *T. gondii*. In the industrialized nations most transmission to human beings probably results from ingestion of undercooked infected meat (particularly lamb and pork). In many areas of the world, about 10 percent of lamb and 25 percent of pork products contain encysted *T. gondii*. In addition, *T. gondii* may be present in certain unpasteurized dairy products, such as goat's milk. More-superficial contamination of food can be effected by flies and cockroaches, which are capable of transporting feces-derived oocysts.

Congenital infection occurs in some nonfeline species but is of greatest concern in human beings. About one-third to one-half of human infants born to mothers who have acquired *T. gondii during that pregnancy* are infected (infection of the fetus is extremely unlikely if the maternal infection occurs before conception). Fetal infection may or may not result in disease. In general, infection of the fetus by *T. gondii* is least common (but disease is most severe) if the maternal infection occurs during the first trimester of pregnancy. Fetal infection is most common (but disease is least severe, often asymptomatic) if the maternal infection occurs during the third trimester. *The vast majority of women infected during pregnancy have no symptoms of the infection themselves.* Congenital infection resulting from reactivation of a chronic (cyst) infection in the mother appears to be exceedingly rare.

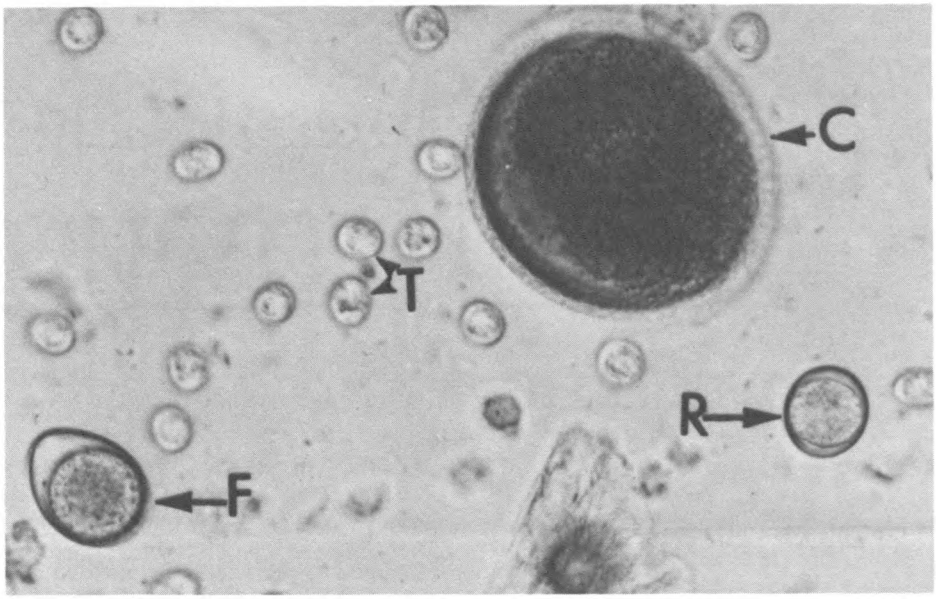

Fig. 1. Unsporulated oocysts of *Toxoplasma gondii* (T), *Isospora felis* (F), and *Isospora rivolta* (R), from fecal flotation. The oocysts are compared with an egg of the ascarid worm *Toxocara cati* (C). Unstained, × 410. (From Dubey, J. P.: A Review of *Sarcocystis* of Domestic Animals and of Other Coccidia of Cats and Dogs. *J. Am. Vet. Med. Assoc. 169:* 1061–78, 1976. Reprinted with permission. Courtesy of Dr. J. P. Dubey, USDA/ARS.)

Clinical Signs of Toxoplasmosis in Cats

In most instances cats show no clinical signs of infection by *T. gondii*. The organism proliferates in the bowel, oocysts are excreted in the feces for a short period of time, tissue cysts are formed, and then the active infection is effectively terminated by the immune response. Occasionally, however, clinical disease (toxoplasmosis) in cats is seen.

The development of toxoplasmosis is age related; kittens and young adult cats are more often affected than older animals. Some cases of toxoplasmosis represent initial infections by the parasite in which the immune response of the host has been unsuccessful, while others are apparently the result of reactivation of tissue cysts. There is no firm evidence for either a breed or a sex predilection in feline toxoplasmosis.

Lethargy, malaise, loss of appetite, and fever are typical early, nonspecific signs. Pneumonia, manifested by respiratory distress of gradually increasing severity, is a hallmark of toxoplasmosis in the cat. Hepatitis (inflammation of the liver) may be seen, resulting in vomiting, diarrhea, prostration, and jaundice. Pancreatitis (inflammation of the pancreas) and lymphadenopathy (enlargement of lymph nodes) may also occur. Toxoplasmosis can also affect the eyes and central nervous system, producing such signs as inflammation of the retina or anterior ocular chamber, abnormal pupil size and responsiveness to light, blindness, ataxia and incoordination, hyperesthesia (heightened sensitivity to touch), personality changes, circling, head pressing, twitching of the ears, difficulty in chewing and swallowing food, seizures, and loss of control over urination and defecation. Unfortunately, toxoplasmosis may mimic a number of other diseases of the cat, such as panleukopenia, lymphosarcoma, and feline infectious peritonitis (FIP), thus complicating the diagnosis.

Symptoms of Toxoplasmosis in Human Beings

The most serious consequences of toxoplasmosis in human beings involve infection of the fetus or an immunocompromised individual. Healthy, immunocompetent persons usually have few symptoms of infection; when present, the symptoms are most often mild and self-limiting in nature.

It has been estimated that *T. gondii* is responsible for more than 3,000 human congenital infections in the United States each year, most of which are asymptomatic. Among symptomatic individuals, symptoms may be present at birth or may first appear weeks, months, or even years later (the majority of clinical cases appearing at puberty, for example, are the result of congenital, rather than recent, infection). Ocular and central-nervous-system disturbances, deafness, fever, jaundice, rash, and respiratory disease, in varying combinations, are among the more common clinical manifestations in those patients.

In immunocompromised persons—those undergoing immunosuppressive

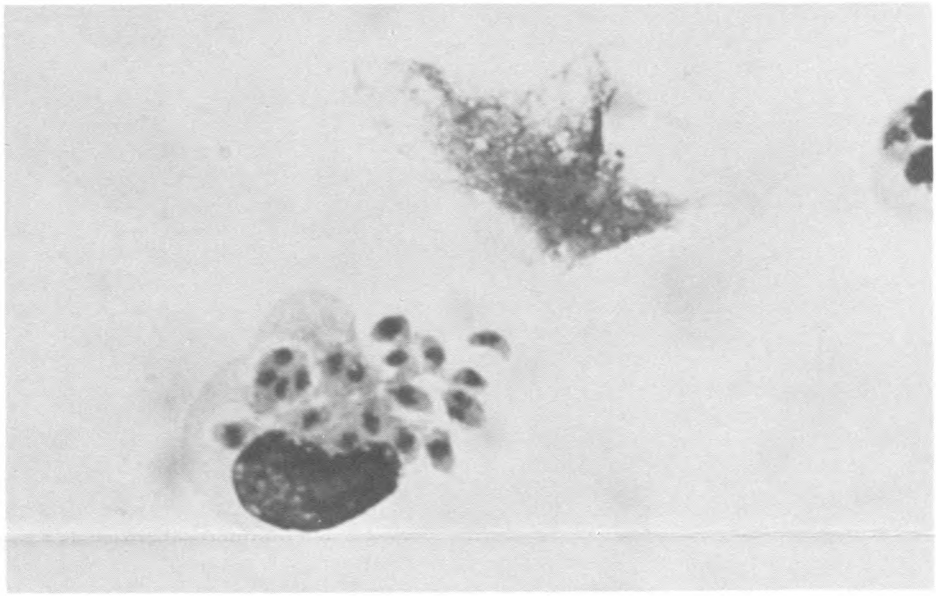

Fig. 2. Impression smear demonstrating release of banana-shaped tachyzoite forms of *Toxoplasma gondii* from an infected cell. Giemsa stain, × 1200. (Courtesy of Dr. J. P. Dubey, USDA/ARS.)

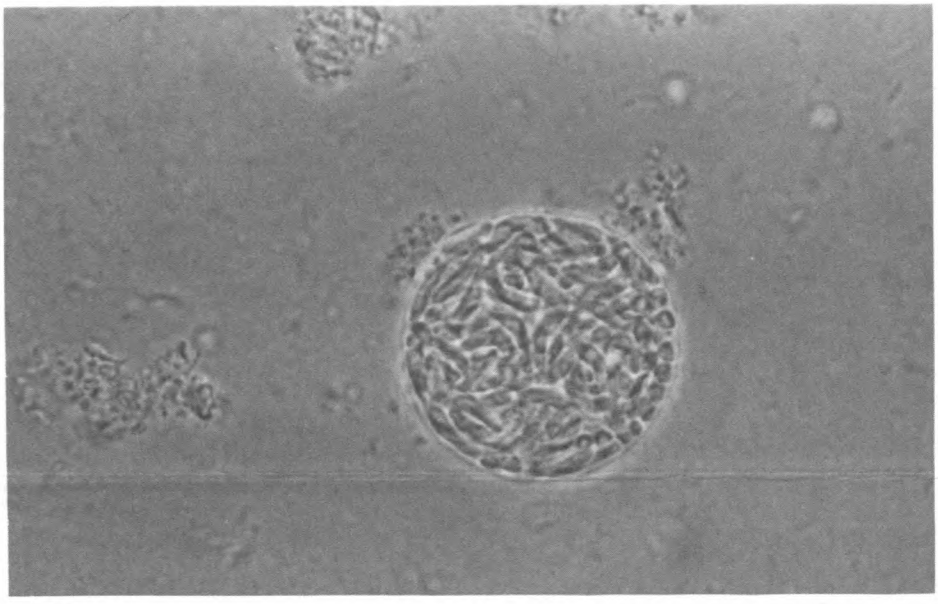

Fig. 3. A tissue cyst of *Toxoplasma gondii*. The cyst wall is thin and encloses numerous bradyzoite forms. Unstained, × 1000. (Courtesy of Dr. J. P. Dubey, USDA/ARS.)

drug therapy (e.g., for cancer or organ transplantation) or those with an immunosuppressive disease such as AIDS—enlargement of the lymph nodes, ocular and central-nervous-system disturbances, pneumonitis, and heart disease are among the more characteristic symptoms. In those patients—especially those with AIDS—relapses of the disease are common, and the mortality rate is high.

(For further information on toxoplasmosis in human beings, see the list of selected general references in this bulletin.)

Diagnosis

The clinical diagnosis of feline toxoplasmosis is made by evaluating the history, presenting signs, and results of supportive laboratory tests. Clinicopathologic procedures important in diagnosis include microscopic examination of tissue, mouse inoculation, serology, and fecal flotation.

Microscopic Examination of Tissue and Mouse Inoculation A *definitive* diagnosis of feline toxoplasmosis requires microscopic examination of tissues (biopsy or necropsy) or tissue-impression smears for distinctive pathologic changes and the presence of tachyzoites, and inoculation of suspect material into laboratory mice. The observation of cysts in tissue in the absence of tachyzoites is *not* diagnostic for toxoplasmosis, because it does not provide evidence of active multiplication of *T. gondii;* the encysted parasites may have no connection with the clinical signs shown by the patient. *Only identification of tachyzoites in the suspect tissue indicates active infection.* The diagnosis can be decisively confirmed by inoculation of suspect material into laboratory mice, which serve as indicator hosts.

Serology A *presumptive* serologic and clinical diagnosis may be made by demonstration of a fourfold or greater increase in antibody titers over a three- or four-week period in a cat with signs suggestive of toxoplasmosis. Because antibodies to *T. gondii* arise relatively slowly in cats and do not reach levels comparable with those seen in some other animals or in human beings, it is inadvisable to attempt correlation of a single titer result with the degree of clinical illness. For instance, a negative titer in an ill cat may mean not that the cat is free of infection but that it is in an early stage of acute infection, before detectable antibodies are produced; serologic retesting in three to four weeks would be required to demonstrate conversion to antibody-positive status. Very young cats frequently are seronegative despite showing clinical signs of toxoplasmosis. Conversely, some cats maintain high levels of *T. gondii* antibody for weeks to months without showing any signs of disease.

The presence of a significant antibody titer in a healthy cat suggests that the cat is most likely immune and *not excreting oocysts;* the absence of antibodies in a healthy cat suggests that the cat is susceptible to infection *and thus would shed oocysts* for one to two weeks following exposure. *The definition of a "significant titer" must be provided by the clinical laboratory performing the test.* A number of different techniques are available for detecting *antibodies to T. gondii,* and levels of significance will vary not only among the different tests but also among the different laboratories. Close cooperation between the veterinarian and the diagnostic laboratory in interpretation of test results therefore is essential.

Fecal flotation Early in infection, before antibody production, the shedding of oocysts may be confirmed by their identification in feces (it must be kept in mind, however, that very few cases of clinical disease occur during the early antibody-negative, fecal examination–positive stage). Oocysts may be concentrated by standard fecal-flotation techniques and observed microscopically (250× or 500× magnification)(see fig. 1). Unsporulated oocysts of *T. gondii* are very tiny (12 μm × 10 μm) and must be distinguished from the larger oocysts of other

coccidian parasites of the cat, such as *Isospora rivolta* (25 μm × 20 μm) and *I. felis* (40 μm × 30 μm). Unfortunately, two other (but rarer) sarcocystid genera infecting cats—*Hammondia* and *Besnoitia*—produce unsporulated oocysts morphologically indistinguishable from those of *T. gondii*.

Treatment

Treatment of healthy antibody-positive cats is unnecessary, because most such cats have developed protective immunologic responses to *T. gondii*. Treatment should be reserved instead for cats showing clinical signs of toxoplasmosis. In many cases—especially in young kittens—the course of the disease can be swiftly fatal, so therapy must be applied aggressively.

Because *T. gondii* is incapable of taking up folic acid (important for cell division) from its environment and thus must synthesize its own, inhibitors of that biosynthetic pathway have been important in therapy. The two drugs that are most commonly used—pyrimethamine (Daraprim) and sulfadiazine (a sulfa drug)—act together to block biosynthesis of folic acid, hence inhibiting multiplication of *T. gondii*. Side effects in the patient may be alleviated by simultaneous administration of folinic acid (as calcium leucovorin or as baker's or brewer's yeast). Because toxoplasmosis therapy inhibits multiplication but does not kill existing parasites, the patient must be treated until the immune response is capable of clearing the infection (weeks). Therapy must be initiated as soon as possible after diagnosis and continued for several days after signs have disappeared. If clinical improvement is not seen within two to three days, the diagnosis of toxoplasmosis should be questioned.

Experience suggests that pyrimethamine may be unpalatable or toxic to some cats, even if given in small amounts. Recently, the antibiotic clindamycin has been reported to be effective in treating feline toxoplasmosis; minimal side effects were observed.

Prevention

General Considerations Destruction of *T. gondii* tissue cysts is achieved by thorough cooking of meat to an internal temperature of 70° C (158° F) for at least fifteen to thirty minutes. Freezing and thawing, salting, smoking, or pickling will not reliably destroy all the cysts in a sample of meat. Restricting the access of pet cats to rodents and birds and offering them only cooked meat, commercially prepared cat food, and pasteurized dairy products should preclude most transmission (human beings, too, should refrain from ingesting uncooked meat and unpasteurized dairy products). Scavenging can be discouraged by placing secure lids on all garbage cans. Cats that are allowed to hunt should wear a bell or other warning device to hinder their effectiveness at capturing prey.

Because excreted oocysts are highly resistant to environmental conditions, and because millions of them may be present in a single stool, the level of contamination of garden soil, flower beds, children's sandboxes, cats' litter boxes, and other areas of loose, moist soil where cats defecate may be significant. Under such conditions transmission of oocysts to human beings can be minimized by the following measures:

- Avoid contact with potentially contaminated soil, or wear rubber gloves during contact, followed by vigorous and thorough washing of the hands with soap and water.
- Cover children's sandboxes to preclude contamination by cats.
- Dispose of feces from litter boxes daily or every other day, to remove oocysts before they sporulate and become infective.
- Control flies and cockroaches.
- Disinfect potentially contaminated litter boxes with scalding water or with dry-heat sterilization (55° C, 131° F). Chemical disinfection is *not* a reliable means of destroying *T. gondii* oocysts.

Human Pregnancy Exposure to *T. gondii* of a pregnant woman or a woman contemplating pregnancy can be minimized by observing the following measures:

- Rare or undercooked meat and unpasteurized dairy products should be excluded from the woman's diet.
- Cats in the household should be tested for antibodies to *T. gondii*. Assuming that an animal is healthy, a significant positive titer indicates that it is most probably immune and not excreting oocysts, and thus would be less likely to be a source of human infection. A healthy antibody-negative cat is most probably susceptible to infection *and would shed oocysts* for one to two weeks after exposure to *T. gondii*. If at all possible, testing of cats should be performed *before* human pregnancy is initiated.
- The woman herself should also be tested for antibodies to *T. gondii*, preferably before becoming pregnant. A positive titer would indicate past infection and lessen the likelihood that congenital transmission would occur should the woman be exposed again to the parasite during pregnancy. An antibody-negative woman would thus be at greater risk of transmitting *T. gondii* to the fetus should she become infected during pregnancy.
- Cats in the woman's household should be protected from infection (or reinfection) by precluding their access to birds, rodents, uncooked meat, and unpasteurized dairy products.
- Even if a cat is antibody-positive and negative on fecal flotation—and hence most likely immune—there exists a *potential* for recrudescence of oocyst shedding (albeit in much smaller numbers than during the initial infection). Therefore, a pregnant woman should refrain from handling litter boxes. For safety, litter boxes should be changed daily or every other day by some other person in the household, to eliminate that potential for accidental infection.
- The woman should refrain from handling or holding close to her face any free-roaming cats. It is possible that the fur or paws could be contaminated with oocysts, which might then be transmitted to the woman by hand-to-mouth contact. Any cat allowed indoors should be kept off the bed, pillows, blankets, or other furnishings used by the woman.
- The woman should refrain from handling any cat showing signs suggestive of illness. It is theoretically possible for an acutely infected cat with pneumonia caused by *T. gondii* to aerosolize infective tachyzoites by sneezing.
- The woman should refrain from gardening or should wear rubber gloves while working with garden soil. Uncooked vegetables, whether grown at home or supplied commercially, should be washed thoroughly before ingestion, in case they have been contaminated by cat feces.
- Vigorous and thorough washing of hands with soap and water following contact with soil, cats, unpasteurized dairy products, and uncooked meat or vegetables should be made routine.

Vaccination There is as yet no vaccine available to prevent either *T. gondii* infection or toxoplasmosis in cats, human beings, or other species. Research in that area is in progress.

Summary

- Cats are the definitive host of the protozoan parasite *Toxoplasma gondii* and are the primary reservoir of *T. gondii* infection throughout the world.
- Cats acquire infection by ingesting any of the three infective stages of the parasite: tissue cyst (containing bradyzoites), oocyst, and tachyzoite. Ingestion of tissue cysts present in infected prey animals or in other raw meat probably represents the most common route by which cats are exposed to *T. gondii*. The intraintestinal infection cycle, culminating in the excretion of oocysts in feces, occurs only in cats; the extraintestinal infection cycle, culminating in formation of cysts in the tissues, occurs in most animal species susceptible to *T. gondii* infection.
- Contact with oocyst-contaminated soil is probably the major means by which human residents in developing countries are exposed to the parasite. In the industrialized nations most transmission to human beings probably results from ingestion of undercooked infected meat (particularly lamb and pork).
- Congenital infection is rare in cats but is of great concern in human beings. About one-third to one-half of infants born to mothers who have acquired *T. gondii* during that pregnancy are infected. It has been estimated that *T. gondii* is responsible for more than 3,000 human congenital infections in the United States each year. In general, *T. gondii*–induced disease in the fetus is most severe if maternal infection occurs during the first trimester of pregnancy, and least severe (often asymptomatic) if the infection occurs during the third trimester. *The vast majority of women infected during pregnancy have no symptoms of the infection themselves.*
- Human patients with immunodeficiency disease (AIDS) or who are receiving immunosuppressive medication for cancer or organ transplantation are at increased risk for developing severe toxoplasmosis.
- A *definitive* diagnosis of toxoplasmosis in the cat requires microscopic examination of impression smears or tissues for distinctive pathologic changes and the presence of tachyzoites, and inoculation of suspect material into laboratory mice. A *presumptive* diagnosis may be made by demonstration of a fourfold or greater increase in antibody titers over a three- or four-week period in a cat with signs suggestive of toxoplasmosis.
- Treatment involves a number of medications, some of which may be poorly tolerated by the feline patient. A vaccine is not available.
- It is important to remember that *T. gondii* infection is much more common than clinical toxoplasmosis, and that most infected cats and human beings (assuming that they are not immunocompromised) are resistant to the disease-producing effects of the parasite.

Selected General References

Burridge, M. J. 1980. Toxoplasmosis. *Compendium on Continuing Education for the Practicing Veterinarian* 2:233–39.

Dubey, J. P. 1986. Toxoplasmosis. *Journal of the American Veterinary Medical Association* 189:166–70.

Dubey, J. P. 1986. Toxoplasmosis in Cats. *Feline Practice* 16(4):12–26.

Dubey, J. P. 1987. Toxoplasmosis. *Veterinary Clinics of North America (Small Animal Practice)* 17:1389–1404.

Frenkel, J. K. 1982. Common Questions on Toxoplasmosis: Veterinary, Medical, and Public Health Considerations. *Veterinary Medicine/Small Animal Clinician* 77:1188–96.

Frenkel, J. K., and J. Holzworth. 1987. Toxoplasmosis. In *Diseases of the Cat*, ed. J. Holzworth, vol. 1, pp. 369–90. Philadelphia: W. B. Saunders.

Jacobson, R. H. 1980. Toxoplasmosis—Feline Infections and Their Zoonotic Potential. In *Current Veterinary Therapy VII*, ed. R. W. Kirk, pp. 1307–11. Philadelphia: W. B. Saunders.

Remington, J. S., and R. McLeod. 1986. Toxoplasmosis. In *Infectious Diseases and Medical Microbiology*, ed. A. I. Braude, C. E. Davis, and J. Fierer, 2nd ed., pp. 1521–35. Philadelphia: W. B. Saunders.

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About the Cornell Feline Health Center

The ultimate purpose of the Cornell Feline Health Center is to improve the health of cats by developing methods to prevent or cure feline diseases and by providing continuing education to veterinarians and cat owners. The Cornell Feline Health Center is a nonprofit organization supported largely by private contributions. Correspondence may be directed to:

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